radiographs from the healthy cohort. The level of reproducibility was assessed using root-mean square coefficients of variation (RMSCV%).
To determine whether varying anatomic landmark choice affected precision of KA measurement, tibial and femoral rules were aligned such that: i) end points of both rules were placed at inner or outer cortical edges, ii) midpoint to midpoint distance from centre rule was equal to 10 $\pm$ 0.5 cm or 5.0-7.0 $\pm$ 0.5 cm and iii) femoral rule was aligned parallel to femoral condyles or to tibial plateau. The Bland-Altman analysis method was conducted on data obtained from varying anatomic landmarks (CI = 95%).
Results: Reproducibility analyses revealed a high degree of intraobserver (RMSCV = 0.29%) and interobserver (RMSCV = 0.33%) reproducibility. In test-retest (n = 32, RMSCV = 0.86%) and experience-inexperience (n = 32, RMSCV = 0.61%) experiments, variance was higher than both intra- and interobserver variances but still well under 1% (Table I). Varying the orientation of tibial and femoral rules according to anatomic landmarks did indeed produce a difference that exceeded the *a priori* limit of agreement of -1.55° to 1.65° defined for digital and manual method discrepancy in KA measurement.

Table I. Precision errors in reproducibility analyses of KA measurement

Reproducibility comparisons	Absolute mean difference (°)	RMSSD (°)	RMSCV (%)
Intraobserver	0.56	0.51	0.29
Interobserver	0.66	0.59	0.33
Experience-Inexperience	1.03	1.10	0.61
Test-Retest	1.65	1.55	0.86

Conclusions: Our custom designed software allowed for efficient and rapid measurement of KA in digitized knee radiographs of OA patients. Although test-retest analyses were only performed in a healthy cohort, we anticipate a similar degree of reproducibility in an OA sample, thus allowing assessment of knee OA progression in the clinical research setting. Nevertheless, readers should still be cautious as to employing a standardized set of anatomic landmarks during measurement since the arbitrary selection of landmarks may result in imprecise KA measurement even with digital techniques.

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IMPACT OF COMORBIDITIES ON COMPLAINTS OF EARLY OSTEOARTHRITIS IN THE CHECK STUDY

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Purpose: Osteoarthritis (OA) is the most common diagnosis made in older patients with knee or hip pain in primary care. The prevalence of many other disabling conditions also rises with age, and some chronic conditions can be found together with OA. An important question is whether comorbidity impairs the health of patients with OA. CHECK (Cohort Hip and Cohort Knee)is a prospective multicentre 10- year follow-up study on the onset and progression of OA in participants with early complaints of hip or knee, using the ICF model as a conceptual framework.
Objective: to investigate whether the number of comorbidities is associated with the complaints of participants with early osteoarthritis.
Methods: A participant is included if he has complaints (pain and/or stiffness) of knee and/or hip, is aged 45- 65 years, has never or not longer than 6 months ago visited the general practitioner for these complaints. The collected variables are categorized according to the dimensions of the ICF model. Body functions and structure are measured with the WOMAC (also the limitations in activities), physical examination, standardized radiography of knees and hips and by collecting blood and urine. The influence of the environmental and personal factors are also investigated; the comorbidity (self- reported) and the health related quality of life (SF-36).
Results: 1002 participants are included in 10 center nationwide in the Netherlands with a mean age of 56 years. Two hundred and eighty- seven participants(29%) reported no comorbidity, 305 (30%) reported one comorbidity, 200 (20%)reported two comorbidities and 210(21%) at least 3 comorbidities. There was a significant inverse association with the number of comorbidities and the pain, the stiffness and the function subscale of the WOMAC. Spearman's correlation between the number of comorbidities and the WOMAC were respectively: pain -0,210*, stiffness -0,218* and function -0,243* (*p$<$0,001). All dimensions of the SF-36 also have a significant negative correlation with the number of comorbidites. The strongest association between the number of comorbidities and an individual SF-36 dimension was seen for vitality -0,322 (p$<$0,001).
Conclusions: The CHECK study is a cohort of participants with complaints of hip or knee. The complaints pain, stiffness and limitation in activities, measured with the WOMAC disease specific questionnaire, were inversely related to the number of comorbidities. Indicating that participants with more comorbidities have lower (worse) scores than subjects with fewer comorbidities. For a more general insight into the participants health, the SF-36 is used. These results showed an impairment of health related quality of life which was also negatively associated with increasing number of comorbidities.
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REPORT OF DAILY VITAMIN D SUPPLEMENT USE IS NO GUARANTEE OF PROTECTION AGAINST VITAMIN D DEFICIENCY IN KNEE OSTEOARTHRITIS PATIENTS

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Purpose: Many people take vitamin D supplements in order to prevent vitamin D deficiency. However, a number of clinical trials have suggested that typical supplementary doses of vitamin D are not adequate to prevent deficiency. This study examined the relationship between vitamin D supplementation and vitamin D deficiency among persons with knee osteoarthritis (OA).
Methods: This cross-sectional study evaluated baseline data from the first hundred patients aged $\geq$ 49 years participating in a clinical trial of knee OA. Information collected included demographic characteristics, daily vitamin D supplement intake, weight and height and month of blood draw. Serum 25(OH)D level was measured using liquid chromatography/tandem mass spectrometry. Vitamin D deficiency was defined by serum 25(OH)D $<$ 30 ng/ml. Multivariate logistic regression models were used to identify factors associated with vitamin D supplement intake and vitamin D deficiency. Gender, age, race, education, and BMI were included in all analyses.

Results: The study included 65 women and 35 men, with 77% being White, 18% African American, 2% Asian, and 3% Other. Mean age of the subjects was 63.5 years (± 8.7). 54% of the subjects reported daily vitamin D supplementation, with 31% taking <400 IU vitamin D and 23% taking ≥400 IU. Mean baseline serum (OH)D level was 31.6 (± 12.6) ng/ml, with 47% of subjects found to be vitamin D deficient. Many subjects were vitamin D deficient in spite of supplementation (42% who took ≤400 IU vitamin D, and 30% of those taking >400 IU vitamin D). However, after adjustment for age, gender, race, BMI, education, and month of blood draw, vitamin D supplementation was associated with decreased risk of vitamin D deficiency (subjects taking 1-400 IU vitamin D vs. no-taking, OR = 0.51, 95% CI, 0.16-1.63; subjects taking >400 IU vitamin D vs. no-taking, OR = 0.26, 95% CI, 0.07-1.04), p trend = 0.047. In these models, lower vitamin D levels were inversely associated with education (college graduate or above vs. under, OR = 0.28, 95% CI, 0.09-0.84), and positively associated with African-American race (OR = 4.10, 95% CI, 0.94-18.0).
Conclusions: Many individuals with knee OA are vitamin D deficient in spite of daily vitamin D supplementation. Current recommendation with respect to vitamin D supplementation may require reconsideration for individuals with OA.

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LUMIRACOXIB IMPROVES PAIN AND FUNCTIONAL STATUS IN PATIENTS WITH PRIMARY HIP OSTEOARTHRITIS: A 13-WEEK, MULTICENTER, RANDOMIZED, PLACEBO-CONTROLLED, ACTIVE COMPARATOR TRIAL

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Purpose: Hip osteoarthritis (OA) is a debilitating musculoskeletal disorder, characterized by chronic pain, affecting health related quality of life. Lumiracoxib is a selective COX-2 inhibitor that provides an alternative to traditional NSAIDs for the treatment of OA. The present study was designed to demonstrate the efficacy and safety of lumiracoxib (100 mg od) compared with placebo in patients with primary hip OA. Celecoxib (200 mg od) was used as the positive control.
Methods: The primary efficacy variables included patient's global assessment of disease activity (0-100 mm VAS), WOMAC™ 3.1 LK pain sub-scale score and WOMAC™ difficulty performing daily activities (DPDA) sub-scale score (at Week 13). Prespecified secondary efficacy variables included response to treatment according to Osteoarthritis Research Society International (OARSI) criteria at Weeks 4, 8 and 13; and minimal clinically important improvement (MCII) for hip OA pain by visit. The efficacy in the subgroup of patients ≥65 years was also prespecified to be analyzed for these primary outcomes.
Results: A total of 1262 primary hip OA patients aged ≥40 years (490 were ≥65 years of age) were randomized to receive lumiracoxib 100 mg od (n=427), celecoxib 200 mg od (n=419), or placebo (n=416) over a period of 13 weeks. Lumiracoxib was significantly superior to placebo in all primary efficacy variables and provided similar pain relief compared with celecoxib at 13 weeks (in both overall population and ≥65 years sub group, Table 1). The treatment response in <65 age group was also similar to the overall population and statistically significant compared to placebo.

Table 1. Efficacy of lumiracoxib versus placebo for primary outcomes (estimated difference after 13 weeks)

	Lumiracoxib *vs* Placebo LSM difference (95% CI)	
	Overall Population	≥65 years
Patient's global assessment of disease activity (VAS, mm)	-8.59 (-11.84, -5.33)*	-9.60 (-14.94, -4.25)*
WOMAC™ pain (0-20) scores	-1.12 (-1.63, -0.60)*	-1.63 (-2.48, -0.78)*
WOMAC™ DPDA (0-68) scores	-3.58 (-5.24, -1.91)*	-4.16 (-6.90, -1.42)**

*p<0.001, **p=0.003.

Similar results for all primary endpoints were observed for celecoxib *vs* placebo in the overall population and patients ≥65 years. A greater proportion of patients in the lumiracoxib group (63.0%, 67.0%, 65.8%) had a treatment response according to OARSI criteria at Weeks 4, 8 and 13 compared with placebo (45.4%, 50.0%, 53.6%) and the response was similar to that in the celecoxib group (63.7%, 67.5%, 67.8%). Lumiracoxib and celecoxib were statistically superior to placebo in the achievement of MCII for target hip OA pain after 4 weeks (p≤0.001; p=0.004), 8 weeks (both p≤0.001), and 13 weeks (both p≤0.001) of treatment. The incidence of adverse events in the lumiracoxib, celecoxib and placebo groups was 56.4%, 53% and 47.6%, respectively. The overall percentage of serious adverse events (SAEs) was 1.9%, 1.0% and 2.2% in the respective groups. There were no fatal SAEs in the lumiracoxib and placebo groups. Two deaths occurred in the celecoxib group that were not suspected to be study drug related. Two patients (0.5%) had AST and/or ALT elevations >3 x ULN in the placebo group versus no elevations in the active treatment groups.
Conclusions: Lumiracoxib 100 mg od and celecoxib 200 mg od were well tolerated and provided similar pain relief and improvement in functional status in patients with primary hip OA. Efficacy was maintained in patients ≥65 years.

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IDENTIFYING FACTORS TO PREDICT PLACEBO RESPONDERS IN KNEE OSTEOARTHRITIS CLINICAL TRIALS

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Purpose: The placebo effect is inherent to all treatments. Pharmacotherapy trials assess whether specific effects of an agent are significantly greater than non-specific influences (placebo) on treatment outcomes. In OA trials, rates of placebo response often approach or exceed 50%. Despite this, very little is known about sociodemographic or clinical predictors of placebo response.
Methods: Data were drawn from placebo arm of North American patients in a large clinical trial designed to evaluate the clinical effects of risedronate on knee OA (KOSTAR). OARSI pain criteria (20% and 50% decrease in WOMAC pain) were used to classify participants at 6 months as placebo responders. We examined whether placebo response was associated with baseline demographic, clinical, and radiographic parameters including: age, gender, race, BMI, work status, WOMAC (pain, stiffness, function), patient global assessment, OA at other sites, NSAID, analgesic and glucosamine use, joint space width (JSW) and osteophyte grade.
Results: Of 311 OA patients who started the trial, 269 (86%) completed the 6 month evaluations. Subjects were mostly female (60%) and white (84%) with a mean (± SD) age of 60.4 ± 8.9, BMI of 30.2 ± 5.0, OARSI osteophyte grade of 1.6 ± 0.6 and baseline pain (WOMAC) of 35.1 ± 21.5. Nearly half (49%) reported a 20% decrease in pain while 29% reported a 50% decrease, with no between-group differences by gender or